REMARKS

Status of the Claims

Claims 1-10 and 12-24 are pending in the present application. Claim 11 is canceled. Claims 14, 17-19, and 22-24 are withdrawn as directed to a non-elected invention. Claims 1, 3, 4, and 8 are amended. Support for the amendment to claim 1 is found throughout the application as originally filed including on page 21, lines 5-16 and lines 22-23 and canceled claim 11. Support for amended claim 3 is found, for example, on page 21, lines 5-16, of the originally filed application. Support for amended claim 4 is found on page 33, lines 7-9, in the originally filed application. Claim 8 is amended for clarity to specify "or" in lieu of "and." No new matter is added by way of this amendment. Reconsideration is respectfully requested.

Issues under 35 U.S.C. § 112, Second Paragraph

Claims 1-13, 15, 16, 20, and 21 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite, *see* Office Action, pages 2-3. Applicants respectfully traverse.

Specifically, the Examiner states that the phrase "induction" of a cytotoxic lymphocyte is unclear. In particular, the Examiner states that it is unclear how a cyotoxic lymphocyte can be differentiated from itself. As amended, claim 1 specifies induction "from a precursor cell which can be formed into the cytotoxic lymphocyte." Accordingly, amended claim 1 is not unclear and Applicants respectfully request withdrawal of the rejection.

The Examiner further states that claim 8 is indefinite for reciting "and the cell culture carrier..." in that the parent claim recites "or a cell culture carrier...." Claim 8 is amended to specify "wherein the cell culture equipment is a petri dish, a flask or a bag, or the cell culture carrier is beads, a membrane or a slide glass." Accordingly, amended claim 8 is not unclear and Applicants respectfully request withdrawal of the rejection.

In addition, the Examiner alleges that claim 3 is indefinite for reciting "a cytotoxic lymphocyte containing CD8-positive cell in higher ratio." The Examiner further states that while a population of cells might contain a higher ratio of CD8+ cells in comparison to another cell population, a cytotoxic lymphocyte cannot contain a higher ratio of CD8+ positive cells. Applicants

submit that claim 3, as amended, is not indefinite. Accordingly, withdrawal of the rejection is respectfully requested.

The Examiner further states that claim 4 is indefinite for the recitation "an expansion fold." As amended, claim 4 specifies "a ratio of the number of cells after the expansion to the number of cells before the expansion", in lieu of the phrase "expansion fold." Accordingly, claim 4 is not unclear and Applicants respectfully request withdrawal.

Issues Under 35 U.S.C. § 112, First Paragraph

Written Description

Claims 1-13, 15, 16, 20, and 21 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement, *see* Office Action, pages 3-5. Specifically, the Examiner states that the phrase "fibronectin fragments" is not adequately supported in the instant application. The Examiner believes that the described fragments encompass any fibronectin fragment, such as a fragment comprising only 2 amino acids. The Examiner further states that only type III region fibronectin fragments are specifically described in the present application. In addition, the Examiner notes that the claims do not specify a functional limitation.

As amended, claim 1 specifies "wherein said fibronectin fragment comprises a cell adhesion activity and/or a heparin binding activity." Applicants submit that an ordinary artisan is well aware from the present application and the prior art which amino acid domains are responsible for the described activities. Accordingly, the claims comply with the written description requirement and withdrawal of the rejection is respectfully requested.

Enablement

Claims 1-13, 15, 16, 20, and 21 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement, *see* Office Action pages 4-5. The Examiner states that it is known that the cell binding and heparin binding domain comprising type III repeats are important in the ability of fibronectin to participate in cell adhesion in growth. However, according to the Examiner, it is unclear, for example, how type I domains could be used to prepare cytotoxic lymphocytes.

As noted above, the claims are amended to specify that the fibronectin fragment comprises a cell adhesion activity and/or a heparin binding activity. Accordingly, the claims only encompass fibronectin fragments having functions that the Examiner recognizes could be predictably used in the claimed method. In view of the foregoing, the claims comply with the enablement requirement and withdrawal of the rejection is respectfully requested.

Issues under 35 U.S.C. § 102

Claims 1-13, 15, 16, 20, and 21 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Lamers *et al.*, *Cancer Gene Therapy*, 2002, 9:613:623, ("Lamers"), *see* Office Action, pages 5-6. Specifically, the Examiner alleges that Lamars describes immobilizing fibronectin on a cell culture bag and incubating Peripheral Blood Mononuclear Cells (PBMCs) in a medium containing serum and plasma ranging from 0% to less than 5%. Accordingly, the Examiner believes that Lamers anticipates the instant claims. Applicants respectfully traverse.

Independent claim 1 is directed to a method for preparing a cytotoxic lymphocyte characterized in that the method comprises the step of carrying out at least one step selected from the group consisting of induction from a precursor cell, which can be formed into the cytotoxic lymphocyte, maintenance of a cytotoxic lymphocyte and expansion of a cytotoxic lymphocyte, comprising culturing the precursor cells, which have an ability of differentiating into the lymphocyte, with a medium containing serum and plasma at a total concentration of 0% by volume or more and less than 5% by volume, in the presence of fibronectin, a fragment thereof or a mixture thereof, wherein said fibronectin fragment comprises a cell adhesion activity and/or a heparin binding activity.

Lamars describes activating Peripheral Blood Mononuclear cells (PBMCs) under various conditions: (a) with an anti-CD3 antibody, (b) with an immobilized anti-CD3 antibody and anti-CD28 antibody, or (c) with phytohemagglutin, *see* page 614, right column, lines 27 to 46 of Lamers.

Lamars does not require fibronectin during the activation of PBMCs. Instead, the timing of fibronectin use is during gene transduction, after the activation of T lymphocytes, *i.e.*, after the induction of the cytotoxic lymphocytes, *see* page 615, left column, lines 7 to 17, page 621, right column, lines 42-56. Consequently, cytotoxic activity is improved, *see* Figure 3.

Lamars does not teach the use of fibronectin, even during PBMC culture. Therefore, Lamars fails to describe that activated lymphocytes are obtained using fibronectin. Accordingly, Lamars does not anticipate induction of precursor cells, as described in the instant claims.

Further, Lamars does not anticipate the maintenance of cytotoxic lymphocytes as described in the instant claims. Lamars teaches that T cell lymphocytes are maintained by culturing in RPMI 1640 medium supplemented with 8% human serum, *see, e.g.*, page 622, left column, lines 1-4 of Lamars. In contrast, the instant claims specify that the concentration of serum is between 0% to less than 5%.

In addition, Lamars does not describe "expansion of the cytotoxic lymphocyte" as specified in the instant claims. Lamars teaches the expansion of T lymphocytes by culturing in Mix-Medium. Lamars also never describes the use of fibronectin.

In view of the foregoing, Lamars does not anticipate the instant claims. Withdrawal of the rejection is respectfully requested.

Provisional Non-Statutory Double Patenting Issues

U.S. Application No: 10/486,512

Claims 1-13, 15, 16, 20, and 21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1, 8, 15-18, 28, 30, 32, 34, 36, 37, and 38 of co-pending U.S. Application No: 10/486,512, ('512), in view of Lamers, *see* Office Action, pages 6-7. Applicants respectfully traverse.

The claims in the '512 application are directed to inducing, maintaining, and expanding cytotoxic T cells having antigen-specific cytotoxicity. The method comprises incubating a precursor cell capable of differentiating to a cytotoxic T cell with an antigen presenting cell and the described fibronectin fragments. Accordingly, an antigen presenting cell is a necessary component of the claims in the '512 application. In contrast, the instant claims do not require an antigen presenting cell. Further, the claims in the'512 application do not describe a method, which uses serum and plasma 0-5% by volume in combination with fibronectin. As noted above, Lamars also fails to teach this combination and, accordingly, an ordinary artisan would not have been motivated to combine Lamars with the claims in the '512 application.

In view of the foregoing, the claims are not obvious over the claims of the '512 patent and Lamars. Withdrawal of the rejection is respectfully requested.

U.S. Application No. 10/509,055

Claims 1-13, 15, 16, 20, and 21 are also provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-2, 5-7, 10, 12, 28, 29, 31-35, and 37-39 of co-pending U.S. Application No. 10/509,055, ("'055"), in view of Lamars, *see* Office Action, page 7. According to the Examiner, the '512 application claims a method for inducing, maintaining, and expanding cytotoxic T cells comprising incubating the T cells with fibronectin or a fragment thereof. The Examiner admits that the claims in the'055 application do not describe a medium containing serum and plasma of 0-5% by volume. Nevertheless, the Examiner believes that Lamars remedies these deficiencies.

As noted above, Lamars does not describe a combination of fibronectin or fragments thereof and a medium containing serum and plasma of 0 to less than 5% by volume for inducing precursor cells, which can be formed into the cytotoxic lymphocytes, or maintaining or expanding cytotoxic lymphocytes. Accordingly, an ordinary artisan would not have been motivated to combine Lamars with the claims in the '512 application.

In view of the foregoing, the claims are not obvious over the claims of the '512 patent and Lamars. Withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the above amendment and remarks, Applicants believe the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact L. Parker, PhD, Registration No. 46,046, at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

Dated: MAR 01 2010

Respectfully submitted,

By 46,046

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